

## **REMARKS**

### **The Amendments**

The claims are amended or rewritten to correct informalities mostly pertaining to customary US format and to address the 35 U.S.C. §112 rejections. These amendments do not narrow the scope of the claims. Claim 11, subject to the restriction requirement, is canceled and the subject matter thereof is reserved for filing in a divisional application. The amendments should not be interpreted as an acquiescence to any objection or rejection made in this application.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

### **The Claim Objection**

The objection to claim 12 is believed to be rendered moot by the amendment thereto.

### **The Rejection under 35 U.S.C. §112, first paragraph**

The rejection of claims 17-22 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement is respectfully traversed.

Claims 17-22 have been rewritten as new composition claim 23 and method claims 24-28. It is urged that these claims are adequately enabled by the original disclosure when taken in view of the knowledge of one of ordinary skill in the art. In order to support a rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the burden lies first with the Patent and Trademark Office (PTO) to provide evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. In re Marzocchi et al., 169 USPQ 367 (CCPA 1971). As stated in Marzocchi,

".. a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein..",

and further,

"..it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."  
(emphasis original).

The terms of the instant claims correspond in scope with the disclosure regarding the use of the compounds in "treating a disease associated with proliferative processes" (i.e., claim 24) and specific embodiments of such diseases (i.e., claim 25). See, e.g., the disclosure at page 6, last full paragraph, of the instant specification. Also, the terms of the instant claims correspond in scope with the disclosure regarding the use of the compounds in "treating a primary tumor and/or metastases that are not operatively accessible" (i.e., claims 26-28). See, e.g., the disclosure at the paragraph bridging pages 6-7 of the instant specification. The PTO has failed to provide explanations why it doubts the truth or accuracy of the inventors' statements in their supporting disclosure. The PTO has also failed to provide back up for any such assertions with acceptable evidence or reasoning which is inconsistent with the inventors' statements. The objective evidence of record and known to one of ordinary skill in the art is, in fact, contrary to shedding doubt on applicants' disclosure. See, e.g., the paragraph at the top of page 2 of the disclosure pointing out the knowledge in the art of the very high anti-proliferative activity of epothilone compounds, i.e., the class to which the structure of formula (I) belongs. Such anti-proliferative activity of the epothilone class of compounds was well known to those of ordinary skill in the art; see, e.g., U.S. Patent Nos. 6,982,276 and 7,008,936, as just a view of many examples. There is no evidence to contradict that

applicants epothilone conjugate compounds would be useful in treating diseases associated with proliferative processes and particularly for treating a primary tumor and/or metastases.

The Office Action refers to the so-called "Wands" factors in the enablement rejection. However, applicants submit that a balancing of these factors does not provide the burden of proof necessary for the PTO to make a non-enablement rejection. The applicants have the following comments regarding each factor:

- Breadth of Claims - The scope of the methods treated is no broader than the acknowledged and known activity in the art of epothilones as anti-proliferatives. Further, the scope of the claims as to the nature of the compounds is not addressed and it is pointed out that the scope here is characterized, in part, by the conjugation of the epothilone with a linker-recognition unit.
- State of the Prior Art - As admitted in the Office Action, epothilones are known as antiproliferatives and anti-tumor agents. This factor weighs heavily in support of enablement since it would not involve undue experimentation for one of ordinary skill in the art to use applicants' novel conjugate compounds in methods analogous to the known methods.
- Level of Ordinary Skill - The admitted M.D. or Ph.D. skill level is a very high skill level which also weighs in favor of a finding of enablement.
- Predictability in the Art - Applicants submit that the level of unpredictability is not particularly high given the admitted state of the prior art and the ability of one at a high level of skill in the art to analogously apply applicants conjugate compounds to the known uses of epothilones.
- Direction Provided by Inventor - Applicants disagree that the inventors provided no direction as to the treatment of diseases. As discussed above, the specification points out the known activity of epothilones and the specification exemplifies a number of particular diseases for which an antiproliferative effect is desired.
- Existence of Working Examples - Although there are no working examples of methods of treatment in the disclosure, the law is clear that it is not necessary to provide working examples in order to enable the invention; see, e.g., In re Borkowski, 422 F.2d

904, 164 USPQ 642 (CCPA 1970); and, In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976).

- Quantity of Experimentation Needed - Applicants respectfully submit that the quantity of experimentation needed is not excessive because the type of experimentation that one of ordinary skill in the art would need to conduct is only routine experimentation due to the known activity and uses of the epothilone class and the high level of skill in the art. That some experimentation is required does not support a finding of non-enablement; lack of enablement only arises when the experimentation required is undue.

In applicants' opinion, the above factors do not balance in favor of the PTO meeting its burden of proof to show lack of enablement. Most tellingly, the PTO – which has the burden of proof – provides no evidence or detailed reasoning as to why one of ordinary skill in the art would not have expected applicants' epothilone conjugate compounds to have the same type of activity and utility as was well known to those of ordinary skill in the art for epothilones in general. There is no basis to suggest that one of ordinary skill in the art could not use applicants' epothilone conjugate compounds in methods substantially analogously to methods in which known epothilone compounds are used.

For all of the above reasons, it is urged that the specification viewed in light of the knowledge of one of ordinary skill in the art (a high level here) adequately teaches how to make and use the claimed invention. Thus, the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

#### **The Rejection under 35 U.S.C. §112, second paragraph**

The rejections of claims 1 and 13-20 under 35 U.S.C. §112, second paragraph, are believed to be rendered moot by the above amendments. Claims 13-20 are canceled.


#### **The Rejection under 35 U.S.C. §101**

The rejections of claims 13-16 under 35 U.S.C. §101 is rendered moot by the above amendments canceling these claims.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

  
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Attorney Docket No.: DORRIE-0007

Date: August 7, 2006

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